In re Application of: PATENT
Epstein et al. Attorney Docket No.: MEDIV2010-4

Application No.: 10/618,183 Filed: July 10, 2003

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In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Upon entry of the present amendment, the claims will stand as follows:

Please amend claims 17, 39, 46 and 47 as follows

Please cancel claims 1, 2, 4-8, 13, 14-16, 19, 20-23, 33, 35-38 and 49.

The listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

Claims 1-16 (Cancelled)

17. (Currently Amended) A method for enhancing collateral blood vessel formation in heart or limb muscle tissue, said method comprising:

directly injecting into a site of impaired blood flow in heart or limb muscle tissue an effective amount of a composition comprising early attaching cells obtained [[from]] by culturing autologous bone marrow, which early attaching cells have been transfected in vitro with an adenoviral vector comprising a polynucleotide encoding one or more angiogenic factors selected from hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).

Claim 18 (Cancelled)

19. (Previously Presented) The method of claim 17, wherein the early attaching cells consist essentially of marrow-derived stromal cells and the transfected cells are directly injected into a site of ischemia in the muscle tissue.

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Claims 20-23 (Cancelled)

24 (Previously Presented) The method of claim 47, wherein the period of culturing is from about 3 hours to about 3 days.

25. (Previously Presented) The method of claim 17, further comprising filtering the bone marrow and culturing the bone marrow to obtain the early attaching cells.

Claims 26 - 28 (Cancelled)

29. (Previously Presented) The method of claim 17, wherein the angiogenic factor is selected from a fibroblast growth factor (FGF), a NOS, and PR39.

30. (Previously Presented) The method of claim 17, wherein the angiogenic factor is selected from FGF-1, FGF-2, FGF-4, and FGF-5.

31. (Previously Presented) The method of claim 17, wherein the angiogenic factor is selected from inducible NOS and endothelial NOS.

32. (Previously Presented) The method of claim 17, wherein the angiogenic factor is PR39.

33. (Cancelled)

34. (Previously Presented) The method of claim 17, wherein the method enhances collateral blood vessel formation in the heart or limb muscle tissue.

Claims 35 - 38 (Cancelled)

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39. (Currently Amended) A composition comprising early attaching cells obtained [[from]] by culturing bone marrow, which cells have been transfected with an adenoviral vector comprising at least one polynucleotide that encodes one or more angiogenic factors selected from hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).

- 40. (Previously Presented) The composition of claim 39, further comprising conditioned medium containing one or more of the angiogenic factors expressed from the polynucleotides.
- 41. (Original) The composition of claim 39, wherein the polynucleotide further comprises a transcription regulatory region operatively associated with the polynucleotide.
- (Previously Presented) The composition of claim 39, wherein the transfected cells have been stimulated in vitro by exposure to hypoxia.
- 43. (Previously Presented) The composition of claim 39, further comprising an anticoagulant.
- (Cancelled)
- (Previously Presented) The composition of claim 39, wherein the early attaching cells consist essentially of marrow-derived stromal cells.
- 46. (Currently Amended) The composition of claim 39, wherein the composition is intended to be injected into a patient having ischemic tissue and the early attaching cells are derived from <u>obtained by culturing</u> bone marrow <u>obtained aspirated</u> from the patient.

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47. (Currently Amended) The method of claim 17, further comprising, prior to the injecting, <u>further</u> culturing the early attaching cells in a culture medium to produce conditioned medium containing one or more of the angiogenic factors expressed from the polynucleotide <u>during the further culturing</u>, and wherein the method further comprises injecting <u>into the muscle tissue</u> a <u>composition comprising</u> the one or more angiogenic factors in the conditioned medium along with the transfected <u>early attaching cells</u>.

- (Previously Presented) The method of claim 17, wherein the injecting is at multiple sites in the muscle tissue.
- 49. (Cancelled)